

# Place in the Craniospinal Radiotherapy

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**Abstract** Gliosarcoma (GS) is a rare form of glioblastoma which express simultaneous gliomatous and sarcomatous transformation. Here, we reported a spinal cord gliosarcoma metastatic to spinal cord in a 3 years old boy, and discussed literature.

**Keywords** Child, Gliosarcoma, Spinal Cord Metastasis, Radiotherapy

## 1. Introduction

GS is a rarely seen tumor at childhood. There are two incidence peaks in infantile period and at 10 years of age<sup>1,2</sup>. Contrary to other brain tumors of childhood, it is localized at frontal and temporal lobes in supratentorial area in more than 95% of the cases<sup>3</sup>. On microscopy, biphasic pattern including glial and mesenchymal components is pathognomonic for gliosarcoma<sup>4</sup>.

Clinical behavior and survival are similar to glioblastoma. Prognosis is rather poor despite treatment modalities including surgical resection, radiotherapy, chemotherapy and combination therapies<sup>5,8</sup>. GS has a high recurrence rate as it is a very aggressive tumor. Median survival ranges between 9 and 12 months<sup>1,4</sup>.

Extracranial metastasis is extremely rare in gliosarcoma. In the literature, there are a few pediatric GS cases with extra-cranial metastasis<sup>4</sup>. To best of our knowledge, there is no publication in the literature about spinal cord metastasis of gliosarcoma at thoracic level. Spinal cord metastasis occurs through CSF and it is fatal in almost all cases<sup>5</sup>.

Here, we presented a pediatric gliosarcoma case with spinal cord metastasis, and discussed relevant publications and treatment modalities.

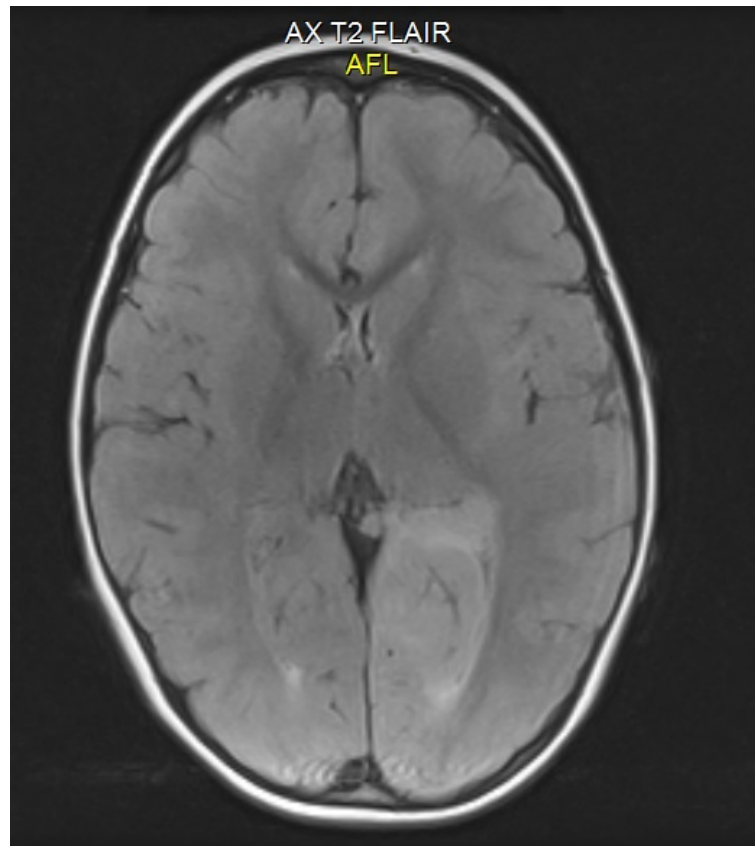
## 2. A Case Report

An otherwise healthy, a 3 years old boy, presented with focal seizure over 3-4 minutes at right arm. There was no fever, vomiting or altered consciousness. On the magnetic

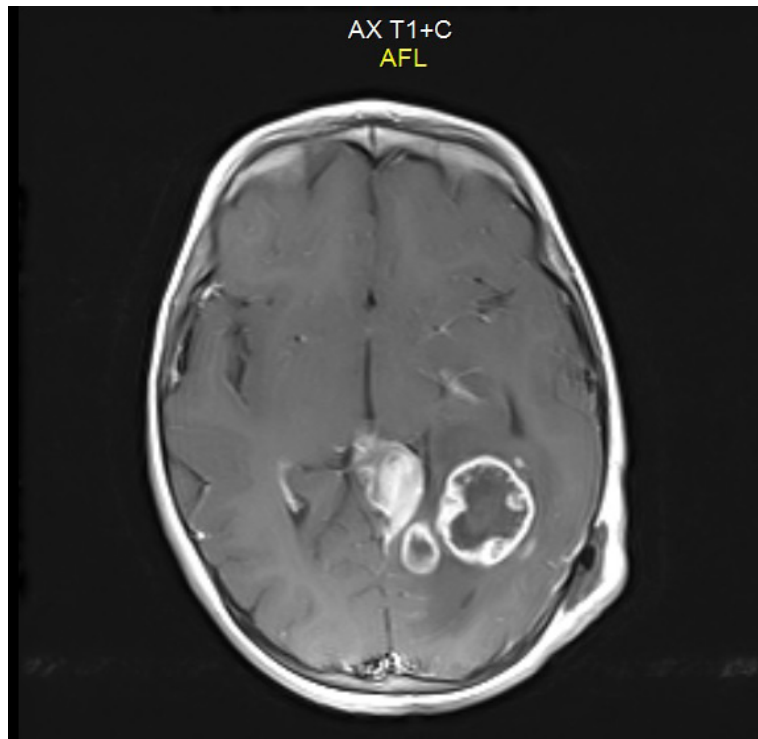
resonance imaging (MRI), there was cortical thickening and increased cortical and sub-cortical signal intensity on T2-weighted images which involved left amygdale, left anterior temporal lob cortex and sub-cortical area and extended up to posterior occipital region (Figure 1). After gadolinium contrast administration, cortical nodular contrast enhancement at left occipital are, slightly increased choline, markedly decreased NAA and lactate peak on magnetic resonance spectroscopy were detected. MELAS syndrome, Rasmussen encephalitis and SSPE were considered in differential diagnosis, but these entities were eliminated as focal nodular contrast enhancement is atypical for these entities; and there was lack of hemorrhage and involvement at contralateral hemisphere. The patient was considered as low-grade glial tumor with recommendation of re-evaluation after 3-months follow-up. However, the patient presented with marked worsening in symptoms one month later. On the MRI, there were mass lesions including a lesion at parietal and occipital region extending from superior margin of tentorium to inferior margin of ventricle at the left (2.7x2.8x3.1 cm in size), another lesion at medial vicinity (1.6x1.1x1.8 cm in size); in addition, multiple lesions with hemorrhage extending to posterior margin of corpus callosum (3.2x1.0x3.4 cm in size) and at adjacent area (3.5x1.7x2.6 cm in size). It was found that there was marked increase in size and number of lesions with contrast enhancement (Figure 2). Stereotactic biopsy was performed at temporal region. Pathological diagnosis was reported as gliosarcoma (grade 4). The patient was discussed at multidisciplinary meeting and it was planned to deliver chemotherapy with vincristine, cyclophosphamide, mesna alternating with temozolomide, carboplatin and etoposide. The patient received a session of methotrexate with a dose of 5 g/m<sup>2</sup>; however, a control MRI was performed due to rapid deterioration in neurological symptoms. As there was an increase in number and size of mass lesions, broad local radiotherapy to cranium was initiated immediately. Spinal MRI was performed to the patient who displayed difficulty in walking on physical examination. However, spinal MRI could be performed 12 days after therapy nodular and linear contrast enhancement (5 mm in size) was observed at thoracic vertebrae 10-12 level, which was interpreted as

spinal seeding (Figure 3). Cranial radiotherapy was withdrawn at the dose of 16 Gy and craniospinal radiotherapy was initiated. Simultaneously, vincristine with a dose of 1 mg/m<sup>2</sup> (weekly) was given to the patient. Radiotherapy was delivered with a total dose of 40 Gy (1.66 Gy fractions per day) in the spinal canal and with a total dose of 40 Gy (1.81 Gy fractions per day) in the cranium. Total dose was completed to 56 Gy for gross mass lesions in the brain and 40 Gy for the spinal metastatic field. No hematological toxicity requiring withdrawal of radiotherapy was observed. Adjuvant chemotherapy was maintained by nimotuzumab and vinblastine. General health status was

markedly deteriorated on the month 3 after radiotherapy. It was found that there was paralysis on 5<sup>th</sup>, 6<sup>th</sup> and 7<sup>th</sup> cranial nerves on physical examination. On MRI, diffuse metastatic foci and mass lesions extending from corpus cavernosum to brainstem were observed. Palliative radiotherapy was initiated directing mass lesions. Radiotherapy was delivered with a total dose of 9.6 Gy (1.60 Gy fractions per day). After palliative radiotherapy, recovery was detected in the paralysis of 5<sup>th</sup> cranial nerve. Chemotherapy was contraindicated due to poor general health status. The patient died 8 months after histopathological diagnosis because of progressive disease.



**Figure 1.** Axial T2-weighted cranial MRI scan shows cortical thickening with increased cortical and sub-cortical signal intensity on the left amygdale and anterior temporal lobe.



**Figure 2.** Axial T1-weighted cranial MRI scan shows enhancing mass lesions on the left parietal and occipital region.



**Figure 3.** Sagittal T1-weighted post-contrast MRI of the thoracic spine demonstrates intramedullary metastatic lesion located at the level of thoracic level vertebra 10-12 (arrows).

### 3. Discussion

Gliosarcoma is the rarest primary malignant tumor of central nervous system in both children and adults. It comprises 2% of pediatric glial tumors. Symptoms vary according to localization and extent of tumor. Most common symptoms are epileptic seizures and dysphasia as majority of gliosarcoma is usually located in the cerebral hemispheres<sup>1,2,5,7</sup>. In the present case, mass localized at parietal and occipital region caused focal epileptic seizure.

To date, 20 GS cases with extracranial metastasis via hematogenous route have been reported in the literature. Majority of these cases were adult patients with cervical cord, lung, liver and lymph node metastasis<sup>4</sup>. In the literature, spinal cord metastasis is extremely rare in GS<sup>2,4</sup>.

In a study, a patient with glioblastoma multiforme (GBM), Pezeshkpour et al. reviewed 18,000 cases with primary central nervous system tumor and reported 18 cases with symptomatic metastasis<sup>6</sup>. This indicated that metastasis occurs at late period after diagnosis of primary tumor. In a study by Grabb et al., 11 cases with metastasis were reported among 33 pediatric cases with malignant glioma. Of these cases, 4 were metastasis of GBM<sup>2</sup>. Packer et al. found metastasis rate as 18% among children with malignant glioma<sup>6</sup>. This can be attributed to improved mean survival due to advances in diagnostic and therapeutic methods.

Recommended treatment is radical excision of mass lesion without interrupting surrounding brain tissue in GS. After surgery, multimodal therapy is employed, including chemotherapy and radiotherapy. In the studies, median survival is found as 6 months in cases underwent surgery alone, while it is found to be prolonged up to 2 years in those received radiotherapy and chemotherapy in addition to surgical excision. Prognosis is rather poor in metastatic gliosarcoma and it is fatal in almost all cases<sup>2,5,7</sup>. In our case, tumor was developed in multiple foci. The disease rapidly progressed and spinal involvement was detected after initiating therapy. No success was achieved in terms of disease progression despite all treatments. Multifocal disease onset made surgery impossible. In the cranium, relapse occurring within radiotherapy field suggested that radiotherapy dose of 40 Gy is insufficient. As spinal cord metastasis was detected during therapy, craniospinal radiotherapy was initiated instead of cranial radiotherapy. Additional radiotherapy doses were delivered to primary lesion and area with seeding. Systemic chemotherapy was

maintained after radiotherapy. However, we could be able to achieve a median survival of 8 months by chemoradiotherapy and adjuvant chemotherapy without surgery.

Gliosarcoma is an extremely rare tumor at childhood, which is localized at cerebral hemisphere and displays high-grade and biphasic pattern. Spinal cord metastasis of primary gliosarcoma is a rarely seen complication of gliosarcoma. If a simultaneous spinal cord metastasis is detected in a patient during treatment of primary intracranial gliosarcoma, treatment should include craniospinal radiotherapy. Adjuvant chemotherapy should be given after radiotherapy. Prognosis is rather poor despite multimodal treatment.

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